

REMARKS

I. Status Summary

Claims 1-27 were filed with the subject application and have been examined by the U.S. Patent and Trademark Office (hereinafter "the Patent Office"). Claims 1-27 have been examined by the Patent Office. Claims 1-27 presently stand rejected.

The Patent Office has objected to the specification upon the contention that the specification fails to comply with the sequence listing requirements.

Claims 11-24 have been rejected under 35 U.S.C. § 112, second paragraph, upon the contention that the claims are indefinite.

Claims 1-10, 17 and 24 have been rejected under 35 U.S.C. § 103(a) upon the contention that the claims are unpatentable over Heron et al. (*The Lancet* 360:851-852 (2002); hereinafter "Heron et al.").

Claims 11, 12, 14-16, 18-23 and 26 have been rejected under 35 U.S.C. § 103(a) upon the contention that the claims are unpatentable over Heron et al. in view of U.S. Patent No. 6,413,719 to Singh et al. (hereinafter "Singh et al.").

Claims 13 and 25 have been rejected under 35 U.S.C. § 103(a) upon the contention that the claims are unpatentable over Heron et al. in view of Claes et al. (2001 *Am. J. Hum. Genet.* 68:1327-1332; hereinafter "Claes et al.").

Claim 27 has been rejected under 35 U.S.C. § 103(a) upon the contention that the claims are unpatentable over Heron et al. in view of Smith et al. (1996 *PNAS* 93:4374-4379; hereinafter "Smith et al.").

Claims 11 and 13-24 have been amended. Support for the amendments can be found throughout the specification as originally filed, and particularly in original claims 11 and 13-24. No new matter has been added.

Claims 11, 12 and 27 have been amended to replace the words "hybridisation", "hybridised", "hybridising", and "hybridise" with "hybridization", "hybridized", "hybridizing", and "hybridize", respectively. Support for these amendments can be found in original claims 11, 12 and 27. No new matter has been added.

Reconsideration of the application based on the arguments set forth herein is respectfully requested.

II. Response to the Objection to the Specification and Notice to Comply

In the instant Official Action and the corresponding Notice to Comply, the Patent Office has objected to the specification upon the contention that the specification fails to comply with the sequence listing requirements. In particular, the Patent Office contends that the primers listed in Table 1 on page 21 of the specification are not accompanied by a sequence identifier.

Without acquiescing to the contentions of the Patent Office applicants respectfully submit that Table 1 on page 21 of the specification as filed has been amended herein such that the primers listed in Table 1 are accompanied by sequence identifiers.

Furthermore, applicants submit herewith a sequence listing in accordance with 37 C.F.R. §§ 1.821-1.825. The sequence listing includes those sequences listed in Table 1.

Accordingly, applicants respectfully submit that the objection to the specification upon the contention that the specification fails to comply with the sequence listing requirements has been addressed. Withdrawal of the instant objection and allowance of the subject application is respectfully requested.

III. Response to the 35 U.S.C. §112, Second Paragraph, Indefiniteness

Claims 11-24 have been rejected under 35 U.S.C. § 112, second paragraph, upon the contention that the claims are indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention. The Examiner contends that "one of the assays" recited in claims 11, 13, 14, 16-20 and 22-24; "the sample DNA to be tested" recited in claim 15; and "said assay" recited in claim 21 lack proper antecedent basis.

After careful consideration of the rejection and the Patent Office's basis therefore, applicants respectfully traverse the rejection and submit the following remarks.

Without acquiescing to the contentions of the Patent Office, applicants respectfully submit that claims 11, 13, 14, 16-20 and 22-24 have been amended to depend from claim 5. Support for the amendments can be found in original claims 11, 13, 14, 16-20 and 22-24 as filed. No new matter has been added. Applicants respectfully submit that claims 11, 13, 14, 16-20 and 22-24 as amended are believed to have proper antecedent basis. As such, applicants respectfully submit that the instant rejection with respect to claims 11, 13, 14, 16-20 and 22-24 is believed to have been addressed.

Without acquiescing to the contentions of the Patent Office, applicants respectfully submit that claim 15 has been amended to depend from claim 5 and recite, *inter alia*, "...wherein one of the assays comprises analysis of SCN2A, KCNQ2 or KCNQ3 genes from a sample DNA from the patient, wherein the sample DNA to be tested is...". Support for this amendment can be found throughout the specification as originally filed and particularly in original claim 15 and at page 7, lines 1-14. No new matter has been added. Applicants respectfully submit that claim 15 as amended is believed to have proper antecedent basis. As such, applicants respectfully submit that the instant rejection with respect to claim 15 is believed to have been addressed.

Without acquiescing to the contentions of the Patent Office, applicants respectfully submit that claim 21 has been amended to recite "said enzymatic assay". Support for this amendment can be found throughout the specification as originally filed and particularly in original claims 20 and 21. No new matter has been added. Applicants respectfully submit that claim 21 depends from claim 20 which recites "an enzymatic assay". As such, claim 21 as amended is believed to have proper antecedent basis. Thus, applicants respectfully submit that the instant rejection with respect to claim 21 is believed to have been addressed.

Taken together, applicants respectfully submit that the rejection of claims 11-24 under 35 U.S.C. § 112, second paragraph, upon the contention that the claims are indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention, has been addressed. Withdrawal of the instant rejection is respectfully requested. A Notice of Allowance is also respectfully requested.

IV. Response to the Rejection of Claims Under 35 U.S.C. § 103(a)

IV.A. Rejection based on Heron et al.

Claims 1-10, 17 and 24 have been rejected under 35 U.S.C. § 103(a) upon the contention that the claims are unpatentable over Heron et al. (*The Lancet* 360:851-852 (2002); hereinafter "Heron et al."). The Patent Office contends that Heron et al. teaches several phenotypic parameters of BFIS, BFNS, and BFNIS diagnosis as well as aspects of mutations in genes that are related to BFNIS and BFNS. The Patent Office admits that Heron et al. does not provide diagnostic methods *per se*. However, the Patent Office contends that it would have been obvious to one of ordinary skill in the art to use the express teachings of Heron et al. regarding the phenotypic parameters of BFIS, BFNS, and BFNIS to develop methods of diagnosing a particular phenotype from among BFIS, BFNS, and BFNIS. The Patent Office further contends that one of ordinary skill in the art would have been motivated to create such diagnostic methodologies based on the teachings of Heron et al. since the skilled artisan would recognize that using the molecular analysis of genes associated with the particular conditions would allow for more accurate diagnosis of distinct phenotypes of similar symptoms.

After careful consideration of the instant rejection and the Patent Office's basis therefore, applicants respectfully traverse the rejection as follows.

Initially, applicants respectfully submit that the reference cited by the Patent Office in support of the instant 35 U.S.C. § 103(a) rejection does not suffice to create a *prima facie* case of obviousness because there is no teaching or suggestion in the reference to make the asserted modifications with a reasonable expectation of success. Particularly, applicants respectfully submit that when the presently claimed subject matter is considered as a whole, Heron et al. cannot be modified to arrive at the presently claimed subject matter without the benefit of hindsight vision. Applicants submit that the cited reference offers no explicit or implicit suggestion to make the modifications suggested by the Patent Office, nor has the Patent Office provided a rationale upon which one of ordinary skill in the art would be motivated to do so, absent

hindsight vision. It appears that the Patent Office is relying on the applicants' disclosure itself to provide the motivation to modify the disclosure of the cited reference to arrive at the instantly claimed invention.

In particular, the Patent Office asserts that it would have been obvious to one of ordinary skill in the art at the time the invention was made to use the teachings of Heron et al. to develop methods of diagnosing a particular phenotype of BFNS, BFIS or BFNIS. However, the Patent Office provides no basis upon which one of ordinary skill in the art would be motivated to modify the teachings of Heron et al. without the benefit of hindsight in view of the instant disclosure. In order to establish a *prima facie* case of obviousness it is not enough for the Patent Office to show that cited reference can be modified. The Patent Office must also establish that the teachings of the cited reference would have motivated a skilled artisan to make the claimed invention with a reasonable expectation of success. As noted by the United States Supreme Court, "The key to supporting any rejection under 35 U.S.C. 103 is the clear articulation of the reason(s) why the claimed invention would have been obvious. *KSR International Co. v. Teleflex Inc.*, 82 USPQ 2d 1385, 1396 (U.S. 2007). No such reason, absent impermissible hindsight, is believed to have been clearly articulated by the Patent Office in support of the instant rejection.

Moreover, applicants respectfully submit that one of ordinary skill in the art would not have had a reasonable expectation of success in modifying the disclosure of Heron et al. to arrive at the presently disclosed subject matter. Heron et al., at best, reports the results of a case study of an Australian family of Irish origin with seven affected individuals and references a previous report of an Ashkenazi Jewish family from Canada comprising six affected individuals. See page 851, left column of Heron et al. The limited scope of the data provided in Heron et al. is not believed to teach one of ordinary skill in the art to arrive at the presently disclosed subject matter with a reasonable expectation of success.

To elaborate, applicants respectfully direct the Patent Office's attention to page 3, lines 3-32 of the subject application as filed, which recites the following:

In 1983, prior to the recognition of BFIS, an American family was reported that had an intermediate variant of BFNS and BFIS, termed benign familial neonatal infantile seizures (BFNIS), where seizure onset varied from 2 days to 3.5 months (Kaplan and Lacey, 1983). Recently, genetic analysis of two BFNIS families lead to the identification of two mutations in the SCN2A gene that were responsible for the disorder (Heron et al, 2002).

The inventors have built on this study through the analysis of affected individuals from additional families with probable or possible BFNIS. This has lead to the identification of further missense mutations in SCN2A in 6 families that result in changes in evolutionary conserved amino acids. Both families clinically recognised as probable BFNIS and four of nine families recognised as possible BFNIS contained SCN2A mutations. This further emphasizes the importance of genetic factors in epilepsies of the neonatal and early infantile periods. Of 95 families with other forms of childhood epilepsy tested, none contained mutations in SCN2A.

The inventors have established a method for the diagnosis of BFNIS and other neonatal and infantile epilepsies, based on testing for the presence of alterations in the SCN2A, and, optionally, the KCNQ2 and/or KCNQ3 genes, in affected patients. The development of a molecular diagnostic test strategy to aid in the diagnosis of neonatal and infantile epilepsies is important. Such a test strategy enables proper management of the affected patient and avoids over-investigation and over-treatment of the patient.

(emphasis added). Further, applicants direct the Patent Office's attention to page 15, lines 9-37 of the subject application as filed, which recites the following:

Prior to the current study, mutations in the SCN2A gene were seen in 2 families with BFNIS. This finding has been expanded upon by the analysis of additional families with early childhood epilepsies so as to refine the molecular-clinical correlation of SCN2A mutations in these epilepsy types.

Example 1: SCN2A mutation analysis in neonatal and infantile epilepsies.

The current study examined three sets of subjects for SCN2A mutations using SSCP analysis and sequencing. These included 2 families with probable BFNIS based on a clinical assessment, nine families with possible BFNIS based on the fact that most individuals had

seizures before 4 months of age and in some families neonatal seizures were observed, and 103 additional families constituting other early childhood epilepsies. In these 103 families, 10 had BFIS, 59 had generalised epilepsy with febrile seizures plus (GEFS+) in whom mutations in SCN1A, SCN1B and GABRG2 were not detected, and 32 constituted unrelated cases with benign childhood epilepsy with centrotemporal spikes.

The results of the mutation analysis of SCN2A in these families showed that missense mutations resulting in changes in evolutionary conserved amino acids were found in a total 6 families. Both families categorized as probable BFNIS, and four of the nine families regarded as possible BFNIS were positive. The mutations in these families were not found in the controls.

(emphasis added). Thus, applicants respectfully submit that the presently disclosed and claimed subject matter is based on the analysis of 114 families. Applicants respectfully submit one of ordinary skill in the art would not have had a reasonable expectation of success in arriving at the presently disclosed and claimed subject matter by modifying Heron et al., which at best pertained to limited data from two families. Accordingly, applicants respectfully submit that the Patent Office has failed to present a *prima facie* case of obviousness because there is no teaching or suggestion in the reference to make the asserted modifications with a reasonable expectation of success.

Thus, applicants respectfully request that the instant rejection of claims 1-10, 17 and 24 under 35 U.S.C. §103(a) be withdrawn at this time. A Notice of Allowance is also respectfully requested.

IV.B. Rejection based on Heron et al. and Singh et al.

Claims 11, 12, 14-16, 18-23 and 26 have been rejected under 35 U.S.C. § 103(a) upon the contention that the claims are unpatentable over Heron et al. in view of U.S. Patent No. 6,413,719 to Singh et al. (hereinafter "Singh et al."). The Patent Office admits that Heron et al. does not teach each and every element of the claims but contends that Singh et al. compensates for the deficiencies.

After careful consideration of the instant rejection and the Patent Office's basis therefore, applicants respectfully traverse the rejection as follows.

Applicants respectfully refer to the discussion hereinabove with regard to the rejection under 35 U.S.C. § 103(a) based on Heron et al. Applicants respectfully submit that the noted deficiencies in Heron et al. are believed to be equally applicable to the instant rejection.

Applicants respectfully submit that Singh et al. fails to compensate for the above-noted deficiencies in Heron et al. As such, applicants respectfully submit that proposed combination of Heron et al. and Singh et al. fails to support a rejection under 35 U.S.C. § 103(a).

Thus, applicants respectfully request that the instant rejection of claims 11, 12, 14-16, 18-23 and 26 under 35 U.S.C. §103(a) be withdrawn at this time. A Notice of Allowance is also respectfully requested.

IV.C. Rejection based on Heron et al. and Claes et al.

Claims 13 and 25 have been rejected under 35 U.S.C. § 103(a) upon the contention that the claims are unpatentable over Heron et al. in view of Claes et al. (2001 *Am. J. Hum. Genet.* 68:1327-1332; hereinafter "Claes et al."). The Patent Office admits that Heron et al. does not teach each and every element of the claims but contends that Claes et al. compensates for the deficiencies.

After careful consideration of the instant rejection and the Patent Office's basis therefore, applicants respectfully traverse the rejection as follows.

Applicants respectfully refer to the discussion hereinabove with regard to the rejection under 35 U.S.C. § 103(a) based on Heron et al. Applicants respectfully submit that the noted deficiencies in Heron et al. are believed to be equally applicable to the instant rejection.

Applicants respectfully submit that Claes et al. fails to compensate for the above-noted deficiencies in Heron et al. As such, applicants respectfully submit that proposed combination of Heron et al. and Claes et al. fails to support a rejection under 35 U.S.C. § 103(a).

Thus, applicants respectfully request that the instant rejection of claims 13 and 25 under 35 U.S.C. §103(a) be withdrawn at this time. A Notice of Allowance is also respectfully requested.

IV.D. Rejection based on Heron et al. and Smith et al.

Claim 27 has been rejected under 35 U.S.C. § 103(a) upon the contention that the claims are unpatentable over Heron et al. in view of Smith et al. (1996 *PNAS* 93:4374-4379; hereinafter "Smith et al."). The Patent Office admits that Heron et al. does not teach each and every element of the claims but contends that Smith et al. compensates for the deficiencies.

After careful consideration of the instant rejection and the Patent Office's basis therefore, applicants respectfully traverse the rejection as follows.

Applicants respectfully refer to the discussion hereinabove with regard to the rejection under 35 U.S.C. § 103(a) based on Heron et al. Applicants respectfully submit that the noted deficiencies in Heron et al. are believed to be equally applicable to the instant rejection.

Applicants respectfully submit that Smith et al. fails to compensate for the above-noted deficiencies in Heron et al. As such, applicants respectfully submit that proposed combination of Heron et al. and Smith et al. fails to support a rejection under 35 U.S.C. § 103(a).

Thus, applicants respectfully request that the instant rejection of claim 27 under 35 U.S.C. §103(a) be withdrawn at this time. A Notice of Allowance is also respectfully requested.

CONCLUSION

In light of the above amendments and remarks, it is respectfully submitted that the present application is now in proper condition for allowance, and an early notice to such effect is earnestly solicited.

If any small matter should remain outstanding after the Patent Examiner has had an opportunity to review the above Remarks, the Patent Examiner is respectfully requested to telephone the undersigned patent attorney in order to resolve these matters and avoid the issuance of another Official Action.

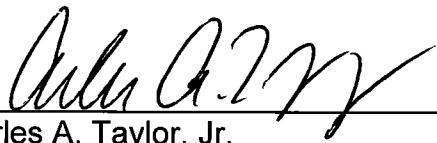
DEPOSIT ACCOUNT

The Commissioner is hereby authorized to charge any deficiency in payment or credit any overpayment of fees associated with the filing of this correspondence to Deposit Account No. 50-0426.

Respectfully submitted,

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Date: 11/12/2009

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